NICOTINE-SEEKING BEHAVIOR IN RHESUS MONKEYS

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Nicotine is known to have psychic dependence potential. In animal experiments, this is demonstrated as the reinforcing effect of nicotine in self-administration of the drug. Several aspects of nicotine-seeking behavior in rhesus monkeys will be discussed in this paper.

1. Characteristics of nicotine-seeking behaviors

In self-administration experiments of nicotine in monkeys, when the monkeys were given free access to nicotine intravenously by pressing a lever switch, their nicotine-seeking behavior appeared mostly during the daytime and each monkey's daily ingested dose was relatively stable (1~4 mg/kg/day). On the other hand, when nicotine was made available in the form of self-administered cigarette smoke, the nicotine-seeking behavior was again observed mostly during the daytime and the serum nicotine levels of some monkeys reached up to 40 ng/ml, but their daily numbers of puffs were relatively erratic (1,000~3,000 puffs/day). It is unclear why nicotine-seeking behavior is stable by the intravenous route yet unstable when ingested by smoking, but some aversive stimuli may be responsibe for the latter.

2. Intensity of nicotine-seeking behavior

As a method to measure the intensity of drug-seeking behavior, a progressive ratio schedule is usually used in self-administration of a drug; the number of lever presses requisite for a drug administration is progressively increased at each drug intake until reaching a breaking point at which the lever pressing is abandoned. Under this schedule with nicotine 0.25 mg/kg/infusion, some monkeys reached final ratios of 2,000~3,000:1. These values can be regarded to be significantly high, although much lower than those for opiates or cocaine. In the case of opiates such as morphine or codeine, it is well known that pretreatment with the drugs prior to the progressive ratio test markedly enhances the drug-seeking behavior, but nicotine pretreatment at hourly doses of 0.25 mg/kg for 4 weeks was not found to enhance the nicotine-seeking behavior.

3. Induction of nicotine-seeking behavior and serum concentration

Intravenous self-administration experiments were conducted at 3 unit doses of nicotine (30, 120, and 240 μg/kg/infusion) in 4 monkeys each in random order. During each 10- to 14-day self-administration period at a fixed unit dose, the serum concentration of nicotine was determined 4 times in each monkey immediately following a lever press and before infusion to find the concentration at which the drug-seeking behavior was induced. As a result, these concentration levels (17.6, 37.3, and 60.1 ng/ml, respectively) were found to be considerably different depending on the daily ingestion level of nicotine (0.9, 2.3, and 4.0 mg/kg/day on the average, respectively). Thus it can be said that the higher the daily ingestion level of nicotine, the higher the serum concentration at which nicotine is sought.

4. Nicotine-seeking behavior and nicotine discrimination behavior

Since drug-seeking behavior is generally believed to be initiated and maintained as a result of reinforcing subjective effects, the dose relationship between the reinforcing effect and discriminating effect of nicotine was examined by observing the intravenous threshold doses in self-administration and drug discrimination experiments in 2 monkeys each. As a result, the threshold unit doses were 15 and 30 μg/kg in the former and 25 μg/kg for both in the latter. This result may indicate that nicotine-seeking behavior is developed as a consequence of its

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